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DEPARTMENT OF THE ARMY
Fort Detrick
Frederick, Maryland

The role of listeria in infectious mononucleosis.

by A. Nyfeldt Landelsforeningens Gigtsanatorium, Skaelskor, Denmark

Discourse No. 8, Listeriosis, a symposium at Giessen, Germany, 27-28 June 1957, pp 86-88. Supplement 1 to Zentralblatt für Veterinärmedizin, 1958.

According to Arneth and Schilling a bacterial infection can be recognized hematologically by leukocytes (neutrophilic phase of defense) with appearance of mature neutrophils (Stabkernige), of neutrophilic metamyelocytes, even of myelocytes. In this phase the eosinophilic leukocytes and the mature hemal monocytes disappear more or less completely. During recovery the eosinophilic leukocytes reappear increasingly (morning redness), followed by lymphocytes and monocytes (recovery phase).

The hematologic changes are quite different, however, in Pfeiffer's glandular fever and in monocytic angina (W. Schultz), especially with a view to angina catarrhalis, follicularis, Plaut-Vincent and diphtheria, in which considerable leukocytosis usually occurs.

For the sake of further descriptions it becomes necessary to explain precisely what we mean by mononucleosis and monocytosis.

Mononucleosis means only one thing, the relative or absolute increase in mononuclear leukocytes in the peripheral blood, while we designate as monocytosis the increase in monocytes in the peripheral blood.

A great number of researchers have dealt with infectious mononucleosis in the past. The first one to recognize it as a nosographical entity was Filatow. He called it "idiopathic lymph-glandular tumescence." Pfeiffer coined the concept of "glandular fever," which was accepted by Hoerschelmann, Korsakoff, Lublinsky, Schleissner and the Dane Kay Schaffer, as well as by the Britons Baldrige, Roher and Hansmann, Beyers, Chapman, Coutts, Fischer, Gilbert and Coleman, Guthrie and Pessel, Mathson, Morse, Neumann, Tidy and Daniel, Tidy and Morse, Park West, and Williams. J. Comby speaks of "Fievre ganglionaire," White, Downey and McKinley of "lymphadenosis" and "acute lymphadenosis," respectively.

Taking their origin more from clinical symptomatology are the designations "acute sublymphatic lymphomatosis," (Turk), "extraordinarily severe lymphocytosis with infection" (Marchand), "sepsis with lymphomatosis" (Cabot), "infection with leukemic hemal aspects" (Nertz), "lymphatic angina" (Koenigsberger), ("lymphoblast-angina" (Preuss), "diphtheroid angina with lymphatic reaction" (Deusding), "angina lymphomatosa" (Ustvedt), "monocytic angina" (Schultz and Baader, Kwansieski and Herring), "lymphomatoid glandular fever" (Glanzmann), "adenitis acuta benigna cum hyperleucocytosis moderata et mononucleosis permagna" (P. Chevallier).

The following designations refer predominantly or exclusively to hematological findings. "Acute infectious increase in blastocytes in the blood with

subsequent recovery" (Hopmann), "hemal aspects of acute leukemia as a temporary symptom" (Klieneberger), "acute, benign leukemia" (Cross), "acute benign lymphoblastosis" (Bloedorn and Houghton), "acute lymphatic leukosis with recovery" (Ireland and Ruhrah as well as Hall).

The most popular and probably the best is the designation "mononucleosis infectiosa," which was first used by Sprunt and Ewans, then by Longcope, Schwenck and Pepper, Tidy and Daniel, Salvsen and Magnusson, Siggaard Andersen and finally by Nyfeldt and Faber.

After publication of Murray, Webb and Swann's "Diseases of rabbits with monocytosis, caused by a heretofore unknown bacterium, *Bacterium monocytogenes*," I started by search in 1929 for a bacterium that could be considered as the cause of human infectious mononucleosis.

After sterile withdrawal of the blood specimen and addition of sterile sodium citrate I allowed the glass to stand for 4 days at room temperature. It was "une faute de mieux" that I left the glass at a room temperature of 18°C and not in the thermostat. Hereby the lysins and opsonins were partially rendered ineffective. During microscopic examination of the leukocytic layer I found small bacteria that had been partly joined to the leukocytic layer and partly ingested by monocytes. I was also able to preserve a primary, pure culture of *Listeria* by means of horse blood agar.

Unfortunately I abandoned this culture method (which later proved excellent) in favor of primary culture with venular blood at 37°C.

I nevertheless succeeded in demonstrating 13 strains of *Listeria*, type III, in patients with mononucleosis in Denmark. In this connection it was peculiar that I was dealing with the heretofore unknown type III after Paterson, which was later also found in other quarters, e.g. East and West Germany, England, USA and Russia.

Much later Stanley of Sidney succeeded in showing that infectious mononucleosis probably has 3 causes:

1. *Listeria monocytogenes*,
2. virus,
3. unknown cause.

With the disclosure of the Paul-Bunell reaction the physician was given the possibility of securing the diagnosis of "infectious mononucleosis."

Based on my extensive examinations I came to the conclusion as early as 1931 that listeriosis would attain a certain importance in human and veterinary medicine.

Hematological findings in the course of a case of infectious mononucleosis with demonstration of listeria:

	Date										
	20/3	21/3	22/3	24/3	25/3	27/3	28/3	29/3	31/3	5/4	
erythrocytes	5070000	-	-	-	5371000	-	-	-	-	4710000	
leukocytes	10440	15310	17910	16110	12300	18310	15870	-	11930	8110	
mature neutrophils(Stabkernige)	2.1%	2.5%	0.5%	0%	4.3%	3.4%	2.7%	1.3%	5.25%	3.2%	
neutrophilic segments	15.5%	7.5%	17.0%	18.5%	27.4%	22.8%	17.9%	30.4%	7.00%	21.2%	
eosinophilic leukocytes	0.1%	0%	0.5%	0%	0%	0%	0%	0%	0%	0%	
basophilic leukocytes	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	
small lymphocytes	10.5%	5.2%	7.3%	6.8%	12.3%	2.3%	2.8%	3.4%	0%	2%	
large lymphocytes	48.8%	47.8%	11.1%	8.3%	49.3%	53.0%	57.3%	18.0%	24.50%	28.4%	
lymphoid monocytes	12.3%	24.7%	30.1%	18.7%	0%	0%	0%	0.2%	10.75%	5.1%	
monocytes	10.7%	12.5%	33.5%	47.4%	6.7%	18.5%	19.5%	46.2%	50.50%	40.1%	
plasma cells	-	-	-	-	-	-	-	-	2.25%	-	
atypical cells	-	-	-	0.3%	-	-	-	-	-	-	
mononuclear cells	82.3%	90.0%	82.0%	81.2%	68.3%	73.8%	79.8%	67.8%	86.75%	75.6%	

NOTES

some
aniso-
cytosis

3
typical
mega-
caryo-
cytes

nuclei of the monocytes show
pronounced polymorphism, some
are purely polynuclear.